#### CLAIMS

### 1. The use of compounds of General Formula I

$$R_1$$
 $R_2$ 
 $R_2$ 
 $R_3$ 
 $(E)\bar{p}$ 
 $(D)n$ 

Formula I

wherein:

X represents O, S;

Y represents H or, along with X, where X = 0, a carbohydrate radical;

A represents N or NR4;

B represents CR5, NR5 or N;

D represents CR6, NR6 or N;

E represents CR7, NR7 or N;

with the condition that the ring containing group A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or double bond;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C<sub>1</sub>-C<sub>6</sub> alkyl, OH, C<sub>1</sub>-C<sub>6</sub> polyhydroxyalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxyl, C<sub>1</sub>-C<sub>6</sub> alkoxyl, C<sub>1</sub>-C<sub>6</sub> alkoxyalkyl, (CH<sub>2</sub>)q-OR', wherein q is 1, 2 or 3, CF<sub>3</sub>, CH<sub>2</sub>-CH<sub>2</sub>F, O-CH<sub>2</sub>-CH<sub>2</sub>F, CH<sub>2</sub>-CH<sub>2</sub>F, CN, NO<sub>2</sub>, O(CO)R', OR', SR', COOR' -SO<sub>3</sub>H, (CH<sub>2</sub>)r-CO<sub>2</sub>R'', (CH<sub>2</sub>)r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or

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substituted phenol group, the possible substituents of the phenol group being any of the meanings of  $R_1-R_7$  except for a phenol group;

R' is H or a  $C_{1-3}$  alkyl group;

R'' is H, a  $C_1$ - $C_6$  alkyl group or a  $C_1$ - $C_6$  alkyloxy group;

with the condition that only one of  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ , X and Y is or has a radioactive isotope;

in the preparation of a composition for diagnosis and/or monitoring of diseases associated with the formation of amyloid protein fibrils, particularly those that appear as amyloid plaques and affect the central nervous system.

## 2. The use of compounds of General Formula II.

Formula II

# wherein:

X represents O, S;

Y represents H or, along with X, where X = 0, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the |||||| line represents a coordinate bond;

A represents N or NR4;

B represents CR5, NR5 or N;

D represents CR6, NR6 or N;

E represents CR7, NR7 or N;

with the condition that the ring containing substituent A has a maximum of two nitrogen atoms

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in its structure;

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m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - - represent a single or double bond;

 $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from:  $C_1$ - $C_6$  alkyl, OH,  $C_1$ - $C_6$  polyhydroxyalkyl,  $C_1$ - $C_6$  alkoxyl,  $C_1$ - $C_6$  alkoxyalkyl,  $(CH_2)$ q-OR', wherein q is 1, 2 or 3,  $CF_3$ ,  $CH_2$ - $CH_2$ F,  $O-CH_2$ - $CH_2$ F,  $CH_2$ - $CH_2$ F, CN,  $NO_2$ , O(CO)R', OR', SR', COOR'  $-SO_3$ H,  $(CH_2)$ r- $CO_2$ R'',  $(CH_2)$ r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of  $R_1$ - $R_7$  except for a phenol group;

R' is H or a  $C_{1-3}$  alkyl group;

R'' is H, a  $C_1$ - $C_6$  alkyl group or a  $C_1$ - $C_6$  alkyloxy group;

with the condition that only one of  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ , X, Y or Z is or has a radioactive isotope;

in the preparation of a composition for diagnosis and/or monitoring of diseases associated with the formation of amyloid protein fibrils, particularly those that appear as amyloid plaques and affect the central nervous system.

3. The use of compounds of General Formula III.

$$R_1$$
 $R_2$ 
 $R_1$ 
 $R_2$ 
 $R_3$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_5$ 
 $R_7$ 
 $R_8$ 
 $R_9$ 
 $R_9$ 

Formula III

#### wherein:

X represents O, S;

Y represents H or, along with X, where X = 0, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the |||||| line represents a coordinate bond;

A represents N or NR4;

B represents CR5, NR5 or N;

D represents CR6, NR6 or N;

E represents CR7, NR7 or N;

with the condition that the ring containing substituent A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or double bond;

 $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from:  $C_1$ - $C_6$  alkyl, OH,  $C_1$ - $C_6$  polyhydroxyalkyl,  $C_1$ - $C_6$  alkoxyl,  $C_1$ - $C_6$ 

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alkoxyalkyl, (CH<sub>2</sub>)q-OR', wherein q is 1, 2 or 3, CF<sub>3</sub>, CH<sub>2</sub>-CH<sub>2</sub>F, O-CH<sub>2</sub>-CH<sub>2</sub>F, CH<sub>2</sub>-CH<sub>2</sub>F, CN, NO<sub>2</sub>, O(CO)R', OR', SR', COOR'  $-SO_3H$ , (CH<sub>2</sub>)r-CO<sub>2</sub>R'', (CH<sub>2</sub>)r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of R<sub>1</sub>-R<sub>7</sub> except for a phenol group;

R' is H or a C<sub>1-3</sub> alkyl group;

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R'' is H, a  $C_1$ - $C_6$  alkyl group or a  $C_1$ - $C_6$  alkyloxy group;

with the condition that only one of  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ , X, Y or Z is or has a radioactive isotope;

in the preparation of a composition for diagnosis and/or monitoring of diseases associated with the formation of amyloid protein fibrils, particularly those that appear as amyloid plaques and affect the central nervous system.

4. Use according to claims 1, 2 and 3 for diagnosis and/or monitoring in animals, transgenic animals, particularly in humans, of diseases such as Alzheimer's, Parkinson's, Huntington, cystic fibrosis, late onset diabetes, neuron disease, Mediterranean fever, Muckle-Wells syndrome, idiopathic myeloma, amyloid polyneuropathy, amyloid cardiomyopathy, senile systemic amyloidosis, hereditary amyloidosis, haemorrhage with Down syndrome, cerebral Creutzfeld-Jacob disease, Kuru, Gerstmann-Straussler-Schienker syndrome, thyroid medullar carcinoma, amyloid valve deposits, amyloidosis in dialysis patients, inclusion body myositis, amyloid muscular deposits, Sickle Cell Parkinson anaemia, type 2 diabetes, amongst others.

## 5. Compounds of General Formula I

$$R_1$$
 $R_2$ 
 $R_3$ 
 $A$ 
 $(B)$ 
 $(E)$ 
 $(D)$ 
 $(E)$ 

#### Formula I

#### wherein:

X represents O, S;

Y represents H or, along with X, where X = 0, a carbohydrate radical;

A represents N or NR4;

B represents CR5, NR5 or N; .

D represents CR6, NR6 or N;

E represents CR7, NR7 or N;

with the condition that the ring containing substituent A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or double bond;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from: C<sub>1</sub>-C<sub>6</sub> alkyl, OH, C<sub>1</sub>-C<sub>6</sub> polyhydroxyalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxyl, C<sub>1</sub>-C<sub>6</sub> alkoxyalkyl, (CH<sub>2</sub>)q-OR', wherein q is 1, 2 or 3, CF<sub>3</sub>, CH<sub>2</sub>-CH<sub>2</sub>F, O-CH<sub>2</sub>-CH<sub>2</sub>F, CH<sub>2</sub>-CH<sub>2</sub>F, CN, NO<sub>2</sub>, O(CO)R', OR', SR', COOR' -SO<sub>3</sub>H, (CH<sub>2</sub>)r-CO<sub>2</sub>R'', (CH<sub>2</sub>)r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of

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 $R_1-R_7$  except for a phenol group;

R' is H or a  $C_{1-3}$  alkyl group;

R'' is H, a  $C_1-C_6$  alkyl group or a  $C_1-C_6$  alkyloxy group;

with the condition that  $R_1,\ R_2,\ R_3,\ R_4,\ R_5,\ R_6,\ R_7,\ X$  and Y are not all simultaneously H, and

with the condition that only one of  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ , X and Y is or has a radioactive isotope;

## 6. Compounds of General Formula II

$$R_1$$
 $A$ 
 $(B)m$ 
 $R_2$ 
 $R_3$ 
 $R_3$ 

Formula II

#### wherein:

X represents O, S;

Y represents H or, along with X, where X = 0, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the |||||| line represents a coordinate bond;

A represents N or NR4;

B represents CR5, NR5 or N;

D represents CR6, NR6 or N;

E represents CR7, NR7 or N;

with the condition that the ring containing group A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or

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double bond;

 $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from:  $C_1$ - $C_6$  alkyl, OH,  $C_1$ - $C_6$  polyhydroxyalkyl,  $C_1$ - $C_6$  alkoxyl,  $C_1$ - $C_6$  alkoxyalkyl,  $(CH_2)$ q-OR', wherein q is 1, 2 or 3,  $CF_3$ ,  $CH_2$ - $CH_2$ F, O- $CH_2$ - $CH_2$ F,  $CH_2$ - $CH_2$ - $CH_2$ F, CN,  $NO_2$ , O(CO)R', OR', SR', COOR' - $SO_3$ H,  $(CH_2)$ r- $CO_2$ R'',  $(CH_2)$ r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of  $R_1$ - $R_7$  except for a phenol group;

R' is H or a C<sub>1-3</sub> alkyl group;

 $R^{\prime\prime}$  is H, a  $C_1-\dot{C}_{\dot{6}}$  alkyl group or a  $C_1-C_6$  alkyloxy group;

with the condition that  $R_1,\ R_2,\ R_3,\ R_4,\ R_5,\ R_6,\ R_7,\ X$  and Y are not all simultaneously H, and

with the condition that only one of  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ , X, Y or Z is or has a radioactive isotope;

### 7. Compounds of General Formula III

$$R_3$$
 $R_3$ 
 $R_4$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_5$ 
 $R_5$ 
 $R_7$ 
 $R_8$ 
 $R_8$ 
 $R_8$ 
 $R_9$ 
 $R_9$ 
 $R_9$ 
 $R_9$ 
 $R_9$ 
 $R_9$ 
 $R_9$ 

Formula III

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#### wherein:

X represents O, S;

Y represents H or, along with X, where X = 0, a carbohydrate radical;

Z represents a metal or rare earth cation that may or may not be radioactive;

the | | | | | | | line represents a coordinate bond;

A represents N or NR4;

B represents CR5, NR5 or N;

D represents CR6, NR6 or N;

E represents CR7, NR7 or N;

with the condition that the ring containing group A has a maximum of two nitrogen atoms in its structure;

m, n and p represent: 0 or 1, where m + n + p = 2 or 3;

the dashed lines - - - represent a single or double bond;

 $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  each independently represent a radioactive isotope, H, a halogen or a radical optionally having a radioactive isotope, said radical being chosen from:  $C_1$ - $C_6$  alkyl, OH,  $C_1$ - $C_6$  polyhydroxyalkyl,  $C_1$ - $C_6$  alkoxyl,  $C_1$ - $C_6$  alkoxyalkyl,  $(CH_2)$ q-OR', wherein q is 1, 2 or 3,  $CF_3$ ,  $CH_2$ - $CH_2$ F, O- $CH_2$ - $CH_2$ F,  $CH_2$ - $CH_2$ - $CH_2$ F, CN,  $NO_2$ , O(CO)R', OR', SR', COOR'  $-SO_3$ H,  $(CH_2)$ r- $CO_2$ R'',  $(CH_2)$ r-CO-R', wherein r is 1, 2 or 3 and Rph, wherein Rph represents a non substituted or substituted phenol group, the possible substituents of the phenol group being any of the meanings of  $R_1$ - $R_7$  except for a phenol group;

R' is H or a  $C_{1-3}$  alkyl group;

R'' is H, a  $C_1-C_6$  alkyl group or a  $C_1-C_6$  alkyloxy group;

with the condition that only one of  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,

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 $R_6$ ,  $R_7$ , X, Y or Z is or has a radioactive isotope;

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and with the condition that when
                A is N;
                B, D and E are all CH,
                X is O, and
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                m, n and p are all 1,
                then R_1, R_2 and R_3 are not all H.
                    Compounds according to claim 5, characterised by
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                being:
                5-chloro-7-[123I]iodo-8-hydroxyquinoline
                5-chloro-7-[124I]iodo-8-hydroxyquinoline
                5-[123I]iodo-7-iodo-8-hydroxyquinoline
                5-iodo-7-[123I]iodo-8-hydroxyquinoline
                5-[124I]iodo-7-iodo-8-hydroxyguinoline
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                5-iodo-7-[124I]iodo-8-hydroxyquinoline
                5-chloro-7-[18F]fluoro-8-hydroxyquinoline
                5-[18F]fluoro-7-iodo-8-hydroxyquinoline
                5-chloro-7-iodo-8-[11C]methoxyquinoline
                5-chloro-7-[123I]iodo-8-hydroxyquinoline glucuronide
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                5-chloro-7-[124I]iodo-8-hydroxyquinoline glucuronide
                5-chloro-7-[18F]fluoro-8-hydroxyquinoline glucuronide
                5-[18F]fluoro-7-iodo-8-hydroxyquinoline glucuronide
                5-chloro-7-iodo-8-[11C]methoxyquinoline glucuronide
                5-[123I]-8-hydroxyquinoline
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               · 5-[124I]-8-hydroxyquinoline
                7-[123I]-8-hydroxyquinoline
                7-[124I]-8-hydroxyquinoline
                5-[18F]-8-hydroxyquinoline
                5-[18F]-8-hydroxyquinoline
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                9. Compounds according to claim 6:
                5-chloro-7-[123I]iodo-8-hydroxyquinoline Fe(II) complex
                5-chloro-7-[123I]iodo-8-hydroxyquinoline Cu(II) complex
                5-chloro-7-[123I]iodo-8-hydroxyquinoline Zn(II) complex
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5-chloro-7-[123I]iodo-8-hydroxyquinoline Mn(II) complex
                5-chloro-7-[124I]iodo-8-hydroxyquinoline Fe(II) complex
                5-chloro-7-[124I]iodo-8-hydroxyquinoline Cu(II) complex
                5-chloro-7-[124]iodo-8-hydroxyquinoline Zn(II) complex
                5-chloro-7-[124I]iodo-8-hydroxyquinoline Mn(II) complex
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                5-chloro-7-[18F]fluoro-8-hydroxyquinoline Fe(II) complex
                5-chloro-7-[18F]fluoro-8-hydroxyquinoline Cu(II) complex
                5-chloro-7-[18F]fluoro-8-hydroxyquinoline Zn(II) complex
                5-chloro-7-[18F]fluoro-8-hydroxyquinoline Mn(II) complex
                5-[18F]fluoro-7-iodo-8-hydroxyquinoline Fe(II) complex
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                5-[18F]fluoro-7-iodo-8-hydroxyquinoline Cu(II) complex
                5-[18F]fluoro-7-iodo-8-hydroxyquinoline Zn(II) complex
                5-[18F]fluoro-7-iodo-8-hydroxyquinoline Mn(II) complex
                5-chloro-7-iodo-8-[11C]methoxyquinoline Fe(II) complex
                5-chloro-7-iodo-8-[11C]methoxyquinoline Cu(II) complex
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                5-chloro-7-iodo-8-[11C]methoxyquinoline Zn(II) complex
                5-chloro-7-iodo-8-[11C]methoxyquinoline Mn(II) complex
                5-chloro-7-iodo-8-hydroxyquinoline 99mTc complex
                5-chloro-7-iodo-8-hydroxyquinoline 111 In complex
                5-chloro-7-iodo-8-hydroxyquinoline 201Tl complex
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                5-chloro-7-iodo-8-hydroxyquinoline 67Ga complex
                5-chloro-7-iodo-8-hydroxyquinoline 68Ga complex
                5-chloro-7-iodo-8-hydroxyquinoline 67Cu complex
                5-chloro-7-iodo-8-hydroxyquinoline 64Cu complex
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                10. Compounds according to claim 7:
                5-chloro-7-[123I]iodo-8-hydroxyquinoline
                                                            Fe(II)
                                                                       bis-
                chelate complex
                5-chloro-7-[123I]iodo-8-hydroxyquinoline
                                                            Cu(II)
                                                                       bis-
                chelate complex '
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                5-chloro-7-[123I]iodo-8-hydroxyquinoline
                                                            Zn(II)
                                                                       bis-
                chelate complex
                5-chloro-7-[123I]iodo-8-hydroxyquinoline
                                                            Mn(II)
                                                                       bis-
                chelate complex
                5-chloro-7-[124I]iodo-8-hydroxyquinoline
                                                            Fe(II)
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                                                                       bis-
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	chelate complex		
. •	5-chloro-7-[124I]iodo-8-hydroxyquinoline	Cu(II) ·	bis-
	chelate complex		•
•	5-chloro-7-[124I]iodo-8-hydroxyguinoline	Zn(II)	bis-
5	chelate complex	,,	
•	5-chloro-7-[124]iodo-8-hydroxyquinoline	Mn(II)	bis-
•	chelate complex		
	5-chloro-7-[18F]fluoro-8-hydroxyquinoline	Fe(II)	bis-
	chelate complex		
10	5-chloro-7-[18F]fluoro-8-hydroxyquinoline	Cu(II)	bis-
	chelate complex		
. •	5-chloro-7-[18F]fluoro-8-hydroxyquinoline	Zn(II)	bis-
	chelate complex		
	5-chloro-7-[18F]fluoro-8-hydroxyquinoline	Mn(II)	bis-
15	chelate complex		
	5-[18F]fluoro-7-iodo-8-hydroxyquinoline	Fe(II)	bis-
	chelate complex		
	5-[18F]fluoro-7-iodo-8-hydroxyquinoline	Cu(II)	bis-
	chelate complex		
20.	5-[18F]fluoro-7-iodo-8-hydroxyquinoline	Zn(II)	bis-
	chelate complex		
	5-[18F]fluoro-7-iodo-8-hydroxyquinoline	Mn(II)	bis-
	chelate complex		
	5-chloro-7-iodo-8-[11C]methoxyquinoline	Fe(II)	bis-
25	chelate complex		
	5-chloro-7-iodo-8-[11C]methoxyquinoline	Cu(II)	bis-
	chelate complex		
	5-chloro-7-iodo-8-[11C]methoxyquinoline	Zn(II)	bis-
	chelate complex		
30	5-chloro-7-iodo-8-[11C]methoxyquinoline	Mn(II) .	bis-
	chelate complex		
	5-chloro-7-iodo-8-hydroxyquinoline 99mTc	bis-che	elate
	complex		
	5-chloro-7-iodo-8-hydroxyquinoline 1111In	bis-che	elate
35	complex		

•	5-chloro-7-iodo-8-hydroxyquinoline	<sup>201</sup> Tl	bis-chelate
	complex		
	5-chloro-7-iodo-8-hydroxyquinoline	<sup>67</sup> Ga	bis-chelate
	complex		•
5	5-chloro-7-iodo-8-hydroxyquinoline	<sup>68</sup> Ga	bis-chelate
	complex		
	5-chloro-7-iodo-8-hydroxyquinoline	<sup>67</sup> Cu	bis-chelate
	complex		
· .	5-chloro-7-iodo-8-hydroxyquinoline	<sup>64</sup> Cu	bis-chelate
10	complex		

- 11. A pharmaceutical composition for diagnosis of diseases associated with protein deposition in the central nervous system comprising one of the compounds defined in claims 5 to 9.
- 12. A method for preparing the compounds defined in claims 5 and 8 comprising:
- a) making a quinoline derivative react with an electrophilic aromatic halogenation reagent incorporating a radioactive halogen atom, or
- b) making a quinoline derivative react with a radioactive halogenated derivative to effect an aromatic nucleophilic substitution reaction.

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- 13. A method for preparing the compounds defined in claims 6 and 9 comprising:
  - a) making a quinoline derivative react with a metal or rare earth cation, or,
  - b) making a quinoline derivative react with a radioactive isotope of these elements

such that the metal or rare earth cation or the radioactive isotope of these elements is in a suitable oxidation state so as to produce the corresponding chelating product defined in claims 6 and 9.

- 14. A method for preparing the compounds defined in claim 7 comprising making a quinoline derivative react with:
  - a) a metal or rare earth cation, or,

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b) a radioactive isotope of these elements.

in a suitable oxidation state so as to produce the corresponding chelating product defined in claims 7 and 10.